PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61B 17/41
A1

(11) International Publication Number: WO 98/52481

(43) International Publication Date: 26 November 1998 (26.11.98)

(21) International Application Number: PCT/GB98/01523

(22) International Filing Date: 26 May 1998 (26.05.98)

(30) Priority Data:
9710562.1 23 May 1997 (23.05.97) GB

(71) Applicant (*for all designated States except US*): MEDICAL LASER TECHNOLOGIES LIMITED [GB/GB]; Unit 4, Belleknowes Industrial Estate, Inverkeithing, Fife KY11 1HY (GB).

(72) Inventor; and
(75) Inventor/Applicant (*for US only*): COLLES, Michael, John [GB/GB]; Boglesknowe, Hartree by Biggar, Lanarkshire ML12 6JJ (GB).

(74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).

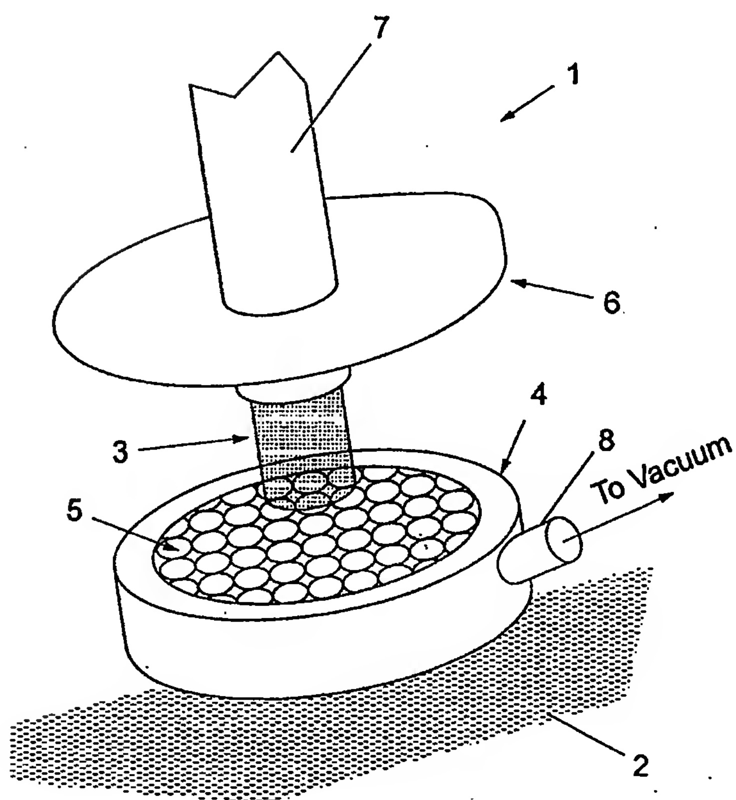
(81) Designated States: AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: APPARATUS AND METHOD FOR DELIVERY OF LIGHT TO SKIN

(57) Abstract

Improvements to a system for the process of hair removal which employs a collimated laser beam delivered to a target. These improvements include a reflector for reflecting back light scattered from the surface and improving light coupling into the tissue, use of an array of micro lenses for focusing the incident beam, and an annular ring to thin the epidermis and upper dennis to reduce blood volume in the illuminated area, and increase flux density at significant depths.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania
AM	Armenia
AT	Austria
AU	Australia
AZ	Azerbaijan
BA	Bosnia and Herzegovina
BB	Barbados
BE	Belgium
BF	Burkina Faso
BG	Bulgaria
BJ	Benin
BR	Brazil
BY	Belem
CA	Canada
CF	Central African Republic
CG	Congo
CH	Switzerland
CI	Cate d'Ivoire
CM	Cameroon
CN	China
CU	Cuba
CZ	Czech Republic
DE	Germany
DK	Denmark
EE	Estonia
ES	Spain
FI	Fmland
FR	France
GA	Gabon
GB	United Kingdom
GE	Georgia
Gil	Ghana
GN	Guinea
GR	Greece
HU	Hungary
IE	Ireland
IL	Israel
IS	Iceland
IT	Italy
JP	Japan
KE	Kenya
KG	Kyrgyzatan
KP	Democratic People's Republic of Korea
KR	Republic of Korea
KZ	Kazakstan
LC	Saint Lucia
LI	Liechtenstein
LK	Sri Lanka
LR	Liberia
LS	Lesotho
LT	Lithuania
LU	Luxembourg
LV	Latvia
MC	Monaco
MD	Republic of Moldova
MG	Madagascar
MK	The former Yugoslav Republic of Macedonia
ML	Mali
MN	Mongolia
MR	Mauritania
MW	Malawi
MX	Mexico
NE	Niger
NL	Netherlands
NO	Norway
NZ	New Zealand
PL	Poland
PT	Portugal
RO	Romania
RU	Russian Federation
SD	Sudan
SE	Sweden
SG	Singapore
SI	Slovenia
SIC	Slovakia
SN	Senegal
SZ	Swaziland
TD	Chad
TC	Togo
TJ	Tajikistan
TM	Turlaneniatan
TR	Turkey
TT	Trinidad and Tobago
UA	Ukraine
UG	Uganda
US	United States of America
UZ	Uzbekistan
VN	Viet Nam
YU	Yugoslavia
ZW	Zimbabwe

Apparatus and method for delivery of light to skin

This invention relates to light delivery and in particular to a apparatus and method for delivery of a beam of light to a target area beneath the surface of the skin.

Most particularly this invention relates to an. apparatus and method designed to improve the delivery of laser or other light to targets underneath the skin surface especially, but not solely, to assist in optical hair removal. That is, this invention relates to the use of optical based techniques in dermatology for the removal of unwanted stains, pigment, marks, hairs, or other sub-surface features.

Lasers and, in some cases, other light sources have found increasing use in dermatology for the treatment or removal of sub-surface lesions. These techniques have largely been based on the concepts of selective photothermolysis•. This implies that the laser wavelength is chosen to match a characteristic absorption associated with the target but not with the surrounding tissue. Thus, absorption of the laser

light and the subsequent heating is largely restricted to that target. In addition, the process also involves choosing the duration of the laser pulse to maximise the temperature of the target before significant conduction to the surrounding tissue can take place. For example, a 30 nanosecond pulse from a Nd:YAG laser at 1.06µm is strongly and selectively absorbed in the blue-black pigments of common tattoos. Since the tattoo pigments accumulate in granules of micron size, such a short pulse is almost wholly used to heat and fragment the granule before significant heating of the surroundings takes place.

More recently techniques have been described which relate to the removal of unwanted hair using lasers. In one approach a Nd:YAG laser similar to the one mentioned above is used. Since there is little or no natural selective absorption at this wavelength, an external chromophore must first be applied and persuaded to migrate down the hair shaft to the base to provide an appropriate target.

In an alternative approach a ruby laser at 0.694nm is used. In this approach the melanin content of the hair shaft provides the selectively absorbing chromophore.

The ruby laser was introduced many years ago for removal of tattoos. For tattoo removal the laser output was "Q-Switched" - that is, the energy was compressed to a pulse of only a few 10's of nanoseconds. Such a pulse, whilst ideal for tattoo granule fragmentation, is neither necessary nor desirable for the more thermal process of hair removal.

For hair removal, the ruby laser is operated in its so-called "normal mode" wherein the pulse duration is

extended to about 1 millisecond. The real target is not the hair itself. Following the selective absorption of the laser light along the buried hair shaft and the heating of the.latter, the overall process relies on the conduction of heat from the shaft to surrounding. tissue, in particular to two zones, the first near the shaft base (papilla); and the second approximately a third of the way down the shaft, known as the bulge. Direct absorption into these zones is possible, and can contribute to their heating since they also contain an enhanced level of melanin. These zones are believed to contain the cells responsible for hair growth, and damage to them via this process of laser heating should lead to permanent hair removal or at least substantially delayed regrowth.

A simple approach is to apply light with the required level of energy density to an area of skin. The level is chosen to give sufficient heating to destroy the target zones whilst leaving the surrounding tissue undamaged. In practice this required level lies between 10 and 50 Jim'.

Various techniques have been used or proposed to assist in improving the efficiency of the process. These techniques include precooling of the area, cooling during the process, selective cooling of the epidermis using millisecond cryogen spray, use of optical transmitting gels to improve coupling into the tissue, convex shaped applicators, and devices to draw folds of skin which may receive radiation from either side.

Whereas there may be both advantages and disadvantages to varying degrees in all of these approaches, it is manifest that there is a need for a beam delivery system that addresses the problems of sub-surface

targeting from both an optical and a biological viewpoint.

According to a first aspect of the present invention there is provided an apparatus for delivery of a beam of light to a target area beneath the surface of the skin comprising means to deliver a collimated light beam, and light delivery means to increase the light energy density at said target area while minimising the light energy density at the surface of the skin.

Preferably said means to improve delivery comprises means to improve effective light coupling into tissue. Said means to improve effective light coupling may comprise recovery means to recover light reflected on incidence with the skin.

Said recovery means may comprise a reflective surface.

Preferably the apparatus comprises means to thin the skin above the target area. Said means may stretch the skin.

Preferably the apparatus comprises means to reduce local blood flow in the target area.

Preferably the means to stretch the skin acts also to reduce the local blood flow.

Preferably the apparatus comprises means to subject the area adjacent the target area to vacuum suction.

Said means may comprise a member adapted to be sealed to the skin and to subject the area of skin surrounding the target area to a vacuum.

Preferably said member has an annular channel. Said channel may be ring shaped or oval. Preferably said channel is adapted to be positioned with the channel opening in contact with the skin.

Preferably the apparatus comprises means to increase light flux density at the depth of the target. Said means may redistribute an incident collimated beam prior to its incidence with the skin.

Said redistribution means may comprise an array of lenses. Preferably said lenses are of short focal length. Preferably said array is selected to increase the flux density at a nominated depth.

Preferably the apparatus comprises recovery means to recover light reflected on incidence with the skin; means to thin the skin above the target; and means to increase light flux at the depth of the target.

Preferably the light beam is a laser light beam.

The apparatus may further include known techniques such as tissue precooling and/or selective cooling of the epidermis and/or use of optical transmitting gels and/or convex shaped applicators and/or devices to draw folds of skin which may receive radiation from either side and/or other features already known.

According to a second aspect of the present invention there is provided a method for delivery of a beam of light to a target area beneath the surface of the skin comprising the step of using an apparatus according to the first aspect of the invention.

According to a further aspect of the present invention

there is provided a method for delivery of a beam of light to a target area beneath the surface of the skin comprising the steps of directing a collimated light beam onto the surface of the skin, and using a light delivery means to increase the light energy density at said target area while minimising the light energy density at the surface of the skin.

Embodiments of the present invention will now be described by way of example only with reference to the accompanying drawings in which:

Figure 1 shows a apparatus in accordance with an aspect of the present invention.

Figures 2a and 2b illustrate the effect on fluence at the skin surface and at a given depth beneath the surface, of increasing the area of surface illumination of the skin;

Figures 2c and 2d also illustrate the effect on fluence at the skin surface and at a given depth beneath the surface, of increasing the area of surface illumination;

Figure 2e is a graphical representation of the rate of increase of the effective fluence at depth with increase of surface beam diameter;

Figures 3a and 3b show a beam focusing arrangements in accordance with an aspect of the present invention;

Figure 4 illustrates means for recapturing reflected light in accordance with an aspect of the present invention; and

Figure 5 shows an annular ring in accordance with an aspect of the present invention.

Referring to the drawings, this apparatus, generally designated 1 is designed to provide a combination of both optical and mechanical means of improvement of the sub-surface flux density of a beam delivered by a beam delivery system to the target areas. Although this apparatus has its origins in improvements related to beam delivery for hair removal, other optical processes requiring selective sub-surface damage may benefit.

A beam delivery system normally comprises a light source and means for its delivery to a target area. A first improvement to this system is the provision of a sealed annular ring 4 as shown in Figure 5. This annular ring is placed adjacent the tissue surface 2 above the target. The region of surface skin in the annulus is subject to a vacuum by connection of a vacuum pump to vacuum outlet 8 and is thus drawn upwards to form raised areas 11. In one dimension this is similar to proposals for obtaining a fold of tissue to allow transillumination. However the instant configuration takes advantage of the fact that dermal blood is taken towards the region 11 under vacuum in the direction of arrows 10 and thus away from the central circular core area 12.

Although the ruby laser wavelength corresponds to a minimum in the absorption spectrum of blood, residual absorption of blood remains a competing unwanted factor in the utilisation of the laser light. Thus reduction of local blood volume due to adjacent vacuum suction provides an important advantage.

A second and more significant effect is that the

drawing up into the annulus of a small amount of tissue 13 effectively stretches the skin 2 throughout the circular core 12. Even mild stretching of around 10% of the diameter - 2mm in Figure 5 where the central area has a diameter of 20mm - translates to a thinning of the epidermis and upper dermis of 20%. Since the reduction in light flux with depth into the skin is exponential this thinning provides an increase in flux density of as much as 80% at a depth of 3mm corresponding to the depth of the papilla. This effect, in conjunction with the reduction of the local blood volume, reduces the required incident flux density by a significant factor. These effects also improve the selectivity of the process.

This aspect of the invention is thus directed principally at providing a physical means of reducing beneficially both the blood content of the tissue immediately below the exposed area, and the thickness through which light must penetrate to reach structures at depths of several millimetres.

Both these effects, that is the biological and the physical, combine to improve the fraction of light fluence (energy per unit area) at the required depth for a given fluence at the surface.

Usually if the target structures are at some significant depth into tissue, a problem arises in trying to balance the need for a minimum fluence at depth required to effect the necessary damage, whilst sparing structures nearer the surface that normally see a significantly higher fluence. This aspect of the invention acts directly to improve this situation and thus helps in sparing surface tissue and components.

A handpiece incorporating such a ring 4 has its most immediate application in a process such as hair removal where selective damage to the follicles 2-4mm deep is required. Other applications, for example the visualisation of dermal blood vessel anatomy for diagnostic purposes would also benefit.

The influence of light scattering in tissue is to substantially increase the volume of tissue experiencing some of the light compared with the initially exposed area. The larger the initial area, the less this affects the fluence at a given depth other than near the perimeter of the area.

This phenomenon is best understood by reference to Figures 2a and 2b.

In Figure 2a the spread of the energy present. in the beam, that is, the expansion of the beam due to scattering, is indicated approximately by following a line 30 representing the average direction of scattered photons. The energy incident on the surface is within an area 20 of $1mm^2$, but at a depth of 3mm 50°s of the incident energy can be found within a much larger area 21 of $1cm^2$. Thus the surface fluence is reduced by about a factor of 200. (This assumes that no absorption takes place.)

If a second area 22, adjacent to the first area 20 and also of 1 mm^2, is illuminated with equal energy, then the fluence (energy density) on the surface remains constant. It can be seen from Figure 2b that at depth the energy from the second source in area 23 very largely overlaps that of the first source in area 21. Thus the fluence at depth has almost doubled for no change in surface fluence.

Figures 2c and 2d show the same effect but with sample fluences typical of laser hair removal.

This process continues with the fraction of the surface fluence effective at depth increasing with size of illuminated area. The rate of increase slows to give a constant fraction when the illuminated area of the surface is several cm'. This function is sketched in Figure 2e, in which line 40 shows the fluence at 3mm depth (in J/cm^2) plotted against the beam diameter at the surface (in mm).

The numbers used in this example are illustrative only but are close to those encountered in skin. In the case of hair removal, a target is approximately 3 mm deep and therefore a certain level of fluence will be' required at that depth to achieve the required therapeutic effect.

This therapeutic fluence is determined by the absorption of light from lasers such as ruby and alexandrite into the melanin within and around the follicle. The epidermis and upper dermis, however, contain the same absorbing chromophore as that present in the target. Since it is desirable to spare the epidermis and upper dermis from damage, and these occur nearer the surface, it is clear that any means by which the ratio of fluence at a depth compared with surface fluence can be increased offers an improvement in efficacy and safety.

An approach taught in current practice is to use large areas of illumination. However this novel approach, and the second aspect of the invention, is to use a lens 15 to sharply focus the incident beam 3 to a point 16 around 3 mm below the surface 2 as shown in Figure

3a. Although there are many scattering events as light moves through the tissue, with the consequences outlined above, each event scatters light in a predominantly forward direction. A sharply focused beam therefore offers some counteraction to the spread induced by scattering.

Unfortunately, to focus the whole beam from a pulsed laser such as ruby or alexandrite presents a serious safety hazard; the slightest incorrect positioning of the focal point would substantially increase the coherent fluence at the surface and lead to severe damage.

Figure 3b shows an arrangement which overcomes this disadvantage by passing the large area collimated beam 3 through an array 5 of small micro lenses 5a. These lenses are of short focal length. The focusing . function of this array 5 is estimated to double the sub-surface flux at point 17. There is insufficient energy falling within the acceptance area of an individual lens 5a to present a safety hazard.

A third aspect of the invention addresses the issue of light coupling into tissue. As mentioned above, the use of a gel has been suggested as a way of improving light coupling. Since the tissue surface is microscopically uneven, applying a gel - and thus essentially smoothing the surface profile to one of near normal incidence to the beam - would indeed help to reduce the reflection losses associated with the refractive index difference between tissue and air. Unfortunately this technique does not really address the reason for the 'apparent' high reflectivity of tissue.

The greater portion of the apparent reflected light is caused not by index mismatch but rather by transmission into the tissue followed by scattering into a backward direction and finally re-emergence.

Although each scattering event is predominantly in the forward direction, there are, on average, some 200 such events per mm penetration. As described earlier some 500 of the incident energy contributes to the fluence at depth whilst the remaining 50% is scattered in all the other directions. A half of this, that is 25% of the total, actually finds its way out of the tissue, contributing to the apparent reflected energy. This figure of 25% is approximate and depends on the nature of the tissue. In skin it can also vary between individuals and on sites on the same individual. However, the figure usually is between 20% and 40%.

This aspect of-the invention seeks to provide means of capturing this effectively reflected light by using a mirror surface 6 around the handpiece 7 and thus returning the light to the tissue surface 2 once more. This is shown in Figure 4. The area of surface that is the source of this back scattered light is larger than the original illuminated area, and the emerging ray directions 18 are spread widely. Under these circumstances, only limited focusing of the light to be returned to the tissue is possible. This is achieved using a mirror surface 6 of a parabolic form. A simpler hemispherical shape or a conical section are alternatives which give adequate advantage. Irrespective of shape, the action of returning the back scattered light to the tissue surface effectively provides an increase in overall coupling, and thus a reduction in the applied energy required to reach a therapeutic level. This reduction is estimated to be

around 20% and therefore an initial requirement of, for example, a fluence of 20 J/cm^2 at the surface 2 would be reduced to around 16 J/cm^2.

In summary, the embodiment shown in Figure 1 shows an apparatus 1 incorporating a combination of the improvements outlined above. This apparatus 1 includes means 4 for drawing up an annulus of tissue, thereby both stretching and thinning the central zone above a target area. This central zone is illuminated with a collimated laser beam 3 passing through an array of micro lenses 5. Typically these lenses may be 1mm in diameter and have a focal length of around 10mm. The delivery handpiece 7 is provided with a means 6 of reflecting back any scattered light returning from the tissue surface.

This embodiment incorporates all the improvements described. Each individual improvement, that is the annular ring 4, the array of micro lenses 5 and the reflector 6 may be separately applied in other simpler embodiments without detracting from their individual ' novelty.

Each individual improvement may also be combined with other established methods such as tissue precooling. Other techniques, for example, for stretching the skin, would be included in the general principles outlined here.

The embodiment described above offers significant advantages to the process of hair removal with lasers or other optical means. Specifically these include a change in the distribution of light to increase the flux density at significant depths of, for example, between 1 and 3 millimetres, a reduction in the blood

volume in the illuminated area and an increase in the effective light flux coupled to the skin. Thus selectivity is improved and the optical energy from the laser or other source is reduced. The embodiment shows specific means for achieving these advantages.

Improvements and modifications may be made to the above without departing from the scope of the invention.

CLAIMS

1. An apparatus for 'delivery of a beam of light to a target area beneath the surface of the skin comprising:

a collimated light beam source; and

light delivery means to increase the light energy density at said target area while minimising the light energy density at the surface of the skin.

2. An apparatus as claimed in Claim 1 wherein said delivery means comprises a reflective surface adapted'to recover light reflected away from the skin on incidence with the skin and to redirect said reflected light towards the skin.

3. An apparatus as claimed in any preceding claim wherein said delivery means comprises means to stretch the skin above the target area.

4. An apparatus as claimed in Claim 3 wherein said delivery means comprises means to subject an area of skin adjacent to the skin above the target area to vacuum suction.

5. An apparatus as claimed in Claim 4 wherein said delivery means comprises an annular channel member adapted to be sealed to the skin.

6. An apparatus as claimed in Claim 5 wherein said channel is ring shaped or oval or of other shape.

7. An apparatus as claimed in Claim 5 or Claim 6 wherein said channel is adapted to be positioned with the channel opening in contact with the skin.

8. An apparatus as claimed in any preceding claim wherein said delivery means comprises means to redistribute an incident collimated beam prior to its incidence with the skin.

9. An apparatus as claimed in Claim 8 wherein said redistribution means comprises an array of lenses.

10. An apparatus as claimed in Claim 9 wherein said lenses are of short focal length.

11. An apparatus as claimed in Claim 9 or Claim 10 wherein said array is adapted to increase the flux density at a predetermined depth.

12. An apparatus as claimed in any preceding claim wherein the light beam is a laser light beam.

13. An apparatus as claimed in any preceding claim further comprising means for precooling the tissue and/or means for selective cooling of the epidermis and/or devices to draw folds of skin which may receive radiation from either side.

14. A method for delivery of a beam of light to a target area beneath the surface of the skin comprising the step of using an apparatus according to any preceding claim.

15. A method for delivery of a beam of light to a target area beneath the surface of the skin comprising the steps of:

directing a collimated light beam onto the surface of the skin; and

using a light delivery means to increase the light energy density at said target area while minimising the light energy density at the surface of the skin.

16. A method as claimed in Claim 15 wherein a reflective surface is used to recover light reflected away from the skin on incidence with the skin and to redirect said reflected light towards the skin.

17. A method as claimed in any of Claims 15 to 16 wherein the skin is stretched above the target area.

18. A method as claimed in Claim 17 wherein an area of skin adjacent to the skin above the target area is subjected to vacuum suction.

19. A method as claimed in Claim 18 wherein a vacuum member comprising an inverted annular channel is placed around the target area and the vacuum member is evacuated to draw the skin into the annular channel.

20. A method as claimed in any one of Claims 15 to 19 wherein said collimated light beam is passed through an array of coplanar lenses positioned above the skin surface.

21. A method as claimed in Claim 20 wherein said lenses are microlenses of short focal length.

22. A method as claimed in Claim 20 or Claim 21 wherein said array is adapted to increase the flux density at a predetermined depth below the skin

surface.

23. A method as claimed in Claim 22 wherein said predetermined depth is between 1 and 5 mm, preferably between 2 and 4 mm.

24. A method as claimed in any one of Claims 15 to 23 wherein the light beam is a laser light beam.

25. A method as claimed in any preceding claim further comprising the steps of precooling the tissue and/or selective cooling of the epidermis and/or use of optical transmitting gels and/or use of convex shaped applicators and/or use of devices to draw folds of skin which may receive radiation from either side.

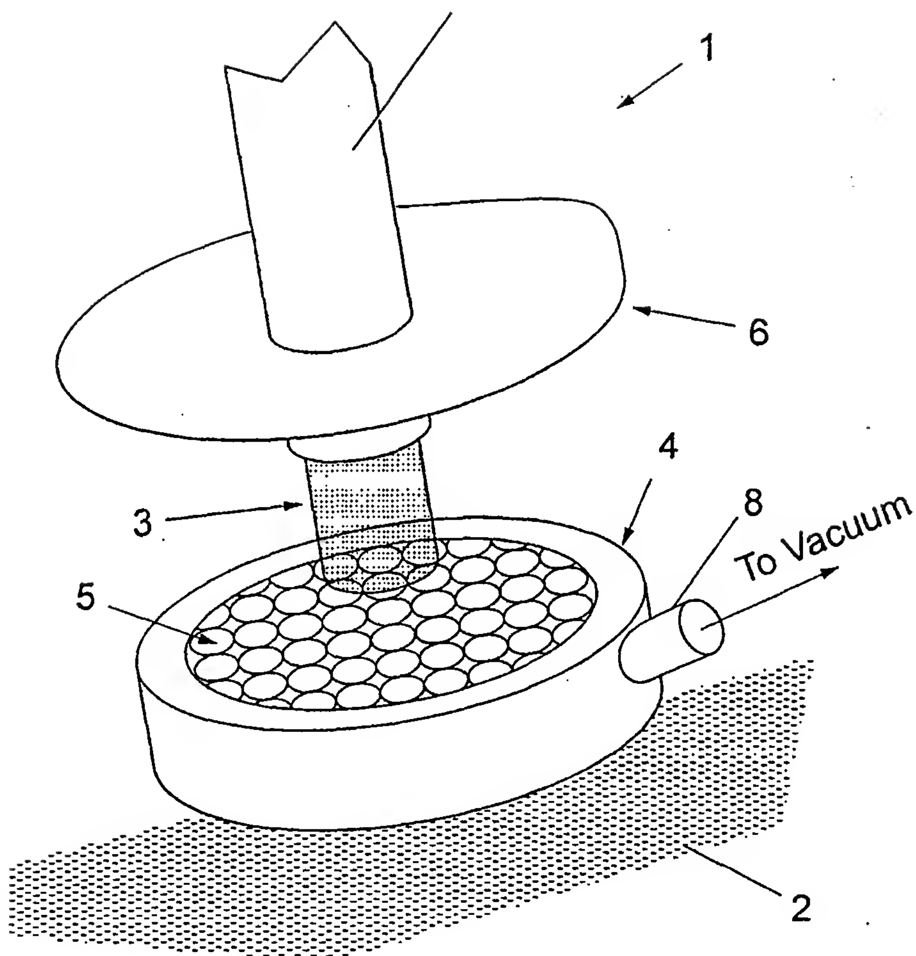


Fig. 1

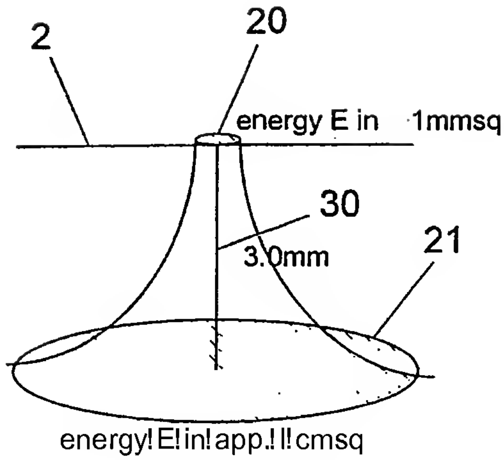


Fig.!2a

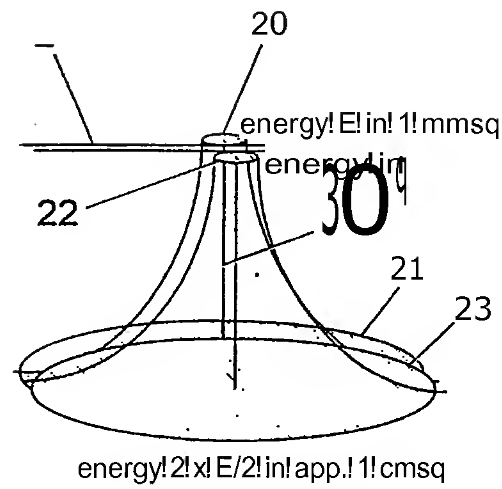


Fig.!2b

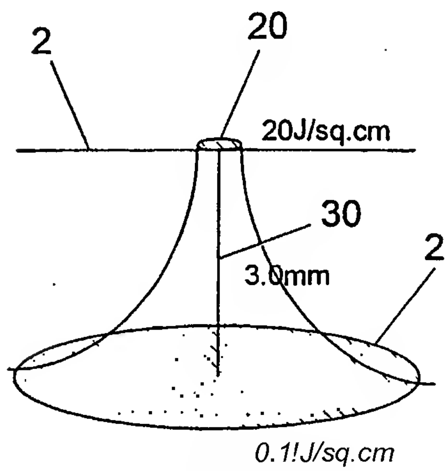


Fig.!2c

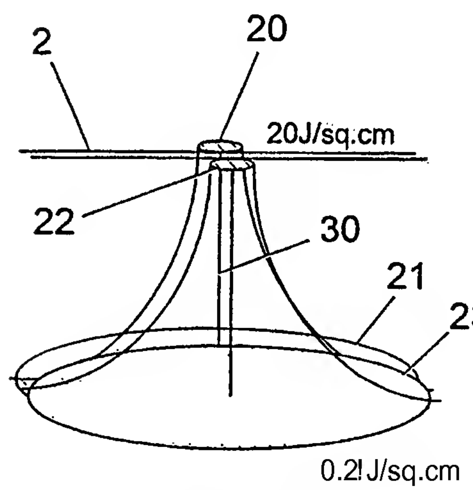


Fig.!2d

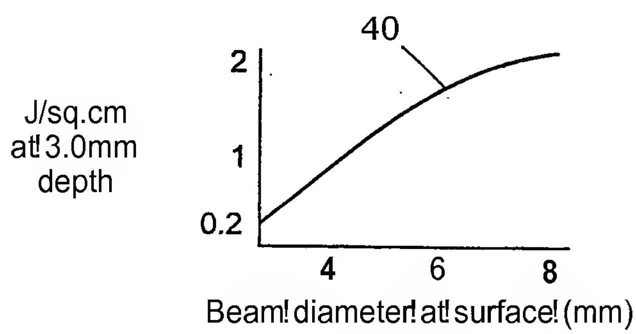


Fig.!2e

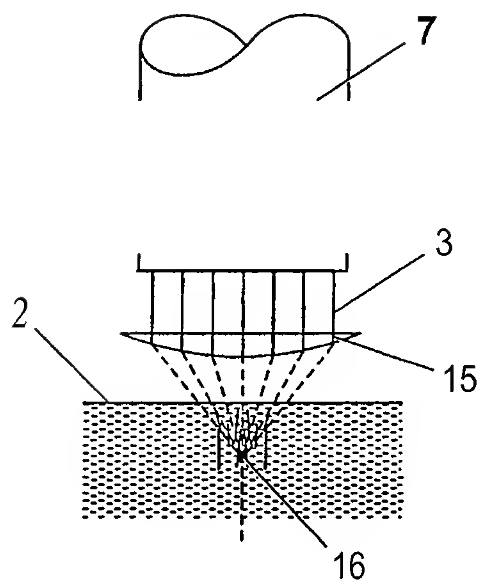


Fig. 3a

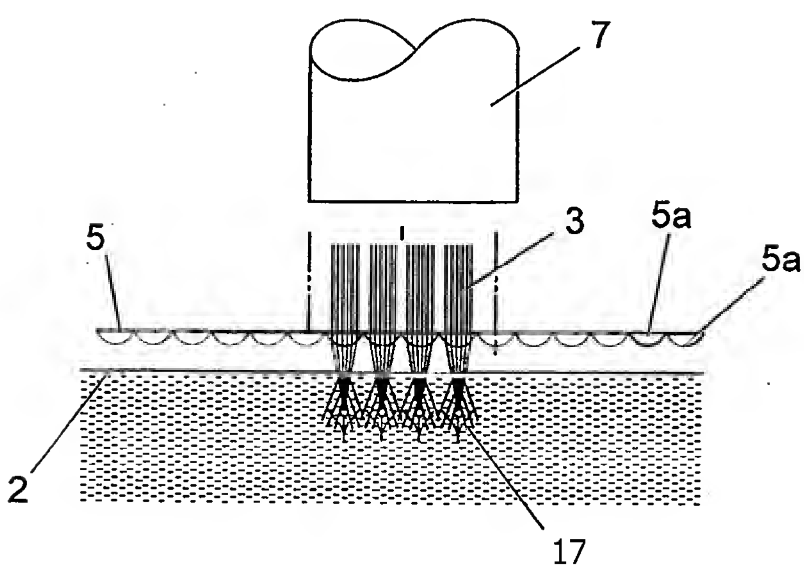


Fig. 3b

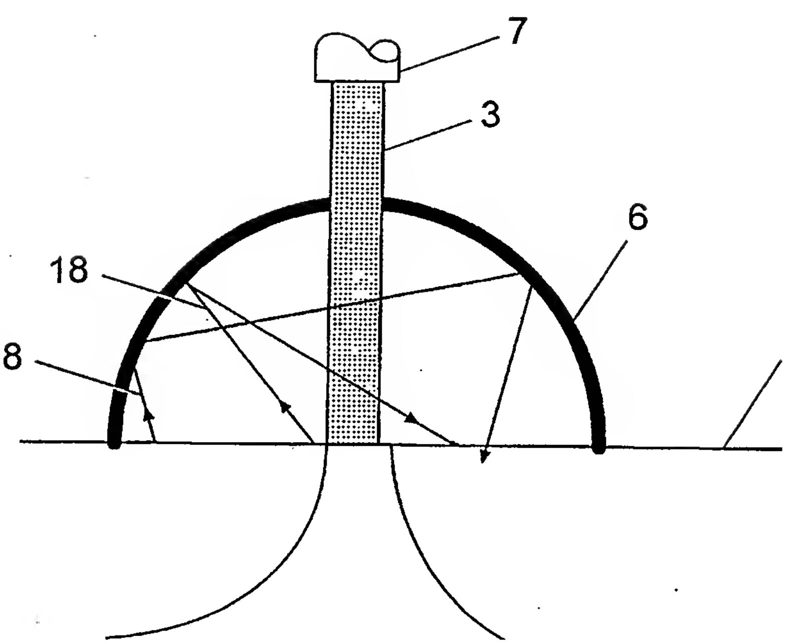


Fig.!4

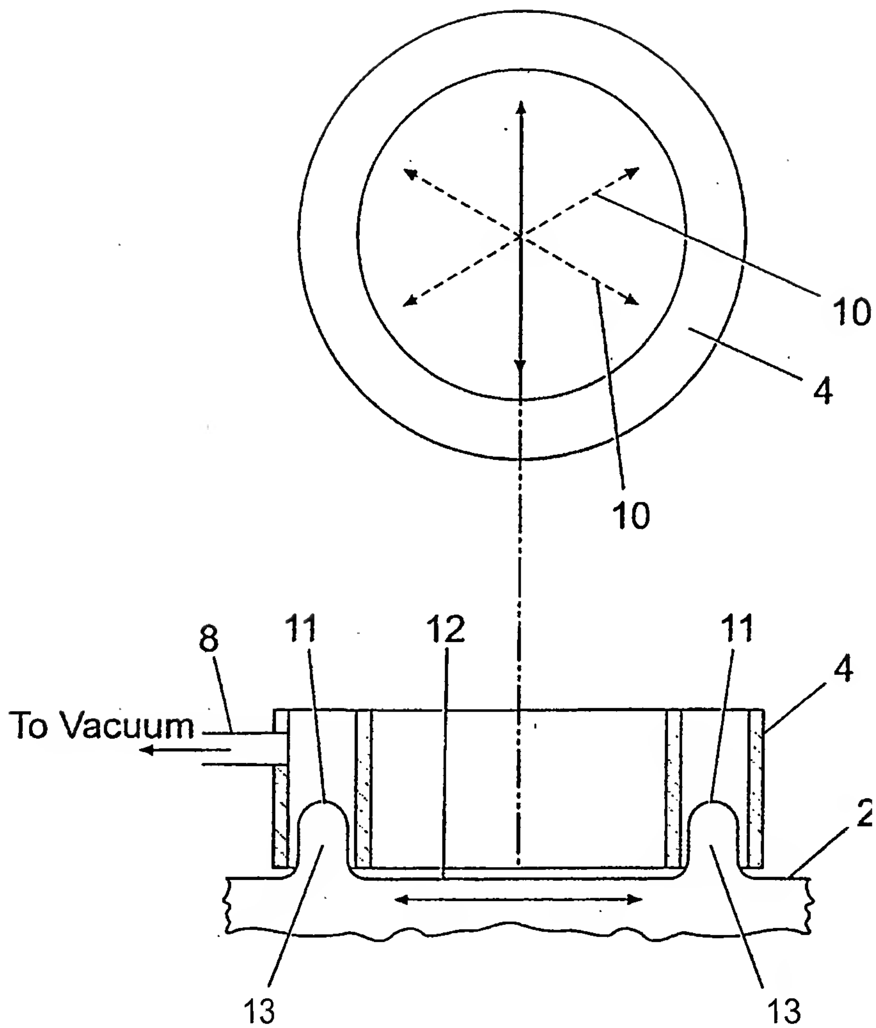


Fig. 5

u'ı 1Lhula! 'tun! AL,! ALAKL! I! KtL'OK1

International Application No
PCT/GB! 98/01523

A. CLASSIFICATION OF SUBJECT MATTER
IPC! 6 A61B17/41

According to International Patent Classification (IPC) or to both national classiNoation and MO

8. FIELDS SEARCHED

Minimum documentation searched (olassiioatlon system followed by olassiioation symbols)
IPC! 6 A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category •	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US! 5! 595! 568! A! (ANDERSON)! 21! January! 1997 see! abstract see! column! 4,! line! 50! -! column! 5,! line! 32 see! column! 4,! line! 50! -! column! 5,! line! 32 see! column! 5,! line! 63! -! column! 6,! line! 21 see! column! 6,! line! 42! -! line! 56	1-3,12, 13
X	US! 5! 546! 214! A! (BLACK)! 13! August! 1996 see! abstract	1,2
X	WO! 84! 02644! A! (WEISSMAN)! 19! July! 1984 see! abstract	1
	-/--	

X Further documents are listed in the continuation of box C.

X Patent family members are listed in annex.

• Special categories of cited documents :

'A' document defining the general stale of the art which is not considered to be of particular relevance

E' earlier document but published on or after the international Ming date

document which may throw doubts on priority olatm(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O' document referring to an oral disclosure, use, exhibition or other means

document published prior to the International filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'%' document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'y document of particular relevance; the claimed invention cannot be coidered to Involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

'8' document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30! July! 1998	QS.oa g

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV New* Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Taccoen,! J-F

2

Form PCTIISA(21c (second sheet((July 1992)

C.Conlinuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of Comment. with indoation,whera appropriate, of the relevant passages	Reliward to claim No.
P,X	US! 5! 735 844 A (ANDERSON) 7 April! 1998 see! abstract;! figures! 2A,2B,3B see! column! 2,! line! 6! -! line! 47 see! column! 5,! line! 21! -! column! 6,! line! 36 see! column! 14,! line! 5! -! line! 67	1-13
P,X	US! 5! 653! 706! A! (ZAVISLAN)! 5! August! 1997 see! abstract see! column! 1,! line! 31! -! line! 52	1-3

2

INTERNATIONAL SEARCH REPORT	International application No. PCT/GB 98/01523

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been eatabliehed in respect of certain claims under Article 17(2)(a) for the following reasons:

1. n Claims Nos.: 14-25
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(4)

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the proscribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search lees were timely paid by the applicant, this International Search Report coirers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional lee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required addtional search lees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[] The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search lees.

I '

tit

INTERNATIONAL SEARCH REPORT

Information on patent family members,..

International Application No
PCT/GB 98/01523

Patent document cited in search report		Publication data	Patent family member(e)		Publication date
US 5595568	A	21-01-1997	CA	2210720 A	08-08-1996
			CN	1172420 A	04-02-1998
			EP	0806913 A	19-11-1997
			WO	9623447 A	08-08-1996
			US	5735844 A	07-04-1998
US 5546214	A	13-08-1996	NONE		
WO 8402644	A	19-07-1984	EP	0134206 A	20-03-1985
US 5735844	A	07-04-1998	US	5595568 A	21-01-1997
			CA	2210720 A	08-08-1996
			CN	1172420 A	04-02-1998
			EP	0806913 A	19-11-1997
			WO	9623447 A	08-08-1996
US 5653706	A	05-08-1997	AU	7401094 A	20-02-1995
			EP	0710136 A	08-05-1996
			JP	9501334 T	10-02-1997
			WO	9503089 A	02-02-1995